REMARKS

The Office Action dated June 29, 2001 has been carefully reviewed and the forgoing amendments are made in response thereto. In view of these amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no prohibited new matter has been introduced by the amendments. While written description support for the amended claims can be found throughout the specification, specific examples of support for the claim amendments can be found as follows:

Claim Amended/Added	Subject Matter	Support in the Specification
Claims 27-35	Exon-intron boundaries	Pg. 5, line 25 - pg. 6, line 5. Original claims 1-10.
Claim 27-45.	SEQ ID NO: 31	Throughout the specification. Original claims 1-10. Sequence listing.
Claims 37-42	Percent sequence identity	Pg. 57, lines 4-26.
Claim 43-44	Stringency conditions	Pg. 61, lines 1 - 4.
Claim 45	Fragments	Pg. 15, lines 6 - 15.

As a result of this amendment, claims 1-10 have been canceled, and claims 27-45 are now under examination.

Response to the objections

Claims 3-10 were objected to for purportedly containing subject matter directed toward a non-elected invention. Applicants have hereby canceled claims 1-10 and each of new claims 27-45 are directed to SEQ ID NO: 31. Applicants respectfully request that this objection be withdrawn in response to the amendment.

The title of the invention was objected to for use of the term "novel" as all patentable inventions are presumed to be novel and non-obvious. Applicants have amended the title of the application to remove the term "novel" and respectfully request that the objection be withdrawn.

Response to the rejection under 35 U.S.C. 101

Claims 1-10 were rejected under 35 U.S.C. 101 purportedly because the claimed invention is not supported by a specific and substantial asserted utility nor a well established utility. As we understand it, the basis of the rejection is that Applicants have purportedly failed to establish a "sequence-to-function" relationship for the claimed sequence. The Office Action asserts that "until some actual and specific significance can be attributed to the nucleic acid identified in the specification as SEQ ID NO: 31 the instant invention is incomplete" (page 4, last paragraph). As explained in detail in the specification and herein, Applicants have clearly established the odorant receptor function for the claimed sequence and that odorant receptors have patentable utility *inter alia* for the identification of agents which modulate odorant receptor activity, as antigens to raise antibodies against the receptors, and in methods to modify insect behavior as set forth in the specification (see, *e.g.*, summary of utility on page 15, lines 25-28). We now address the sequence-to-function issue in detail.

Newly added claims 27-45 are directed to isolated nucleic acid molecules encoded by SEQ ID NO: 31, which is the nucleic acid sequence encoding the odorant receptor known in the specification as DOR22A.1, for *Drosophila* Odorant Receptor No. 22A.1. As discussed in the specification, the designation DOR22A.1 was a tentative designation based on the gene's cytogenetic location in the genome (specification, page 56, lines 11-22). This receptor is now also referred to as DOR22a or Or22a, for Ordorant receptor No. 22a, in the attached declaration of Dr. John Carlson filed under 37 C.F.R. 1.132 ("the Carlson Declaration"). Thus, **DOR22a and Or22a both refer to odorant receptor number 22A.1**, the nucleic acid sequence of which is provided by SEQ ID NO: 31, and the terms "DOR22a" and "Or22a" are used interchangeably in this Amendment and Response. Similarly, DOR22A.2, DOR22b and Or22b all refer to *Drosophila* Odorant Receptor No. 22b, encoded by SEQ ID NO: 1, also mentioned in the

Carlson Declaration and in this response. The genes encoding Or22a and Or22b are tightly linked and highly related (see, *e.g.*, Figure 2.A of the original specification) They encode separate but similar receptors. More specifically, they are located 500 bp apart and are 75% identical at the amino acid level (specification, page 57, lines 6-7).

The specification clearly establishes the biological function of nucleic acid SEQ ID NO: 31 as encoding an odorant receptors (see, *e.g.*, page 58 line 16 through page 59, line 9). The attached Carlson Declaration further demonstrates the biological significance of Or22a/b as odorant receptors. As explained in the Carlson Declaration, the present inventors have shown the following:

1. Antibodies cross-reactive to Or22a and Or22b proteins label dendrites of *Drosophila* olfactory receptor neurons (Carlson Declaration, paragraph 3).
2. Or22a/b expression has the same distribution pattern as ab3 sensilla (Carlson Declaration, paragraph 4).
3. The promoter region of Or22a was used to drive expression of GFP and the expressed GFP was shown to mark the Or22a/b-immunoreactive sensilla (Carlson Declaration, paragraph 5).
4. The recordings from Or22a-GFP sensilla indicate that these labeled sensilla contain two neurons, consistent with either ab2 or ab3; their odor-sensitivities correspond well to those of ab3 (Carlson Declaration, paragraph 6).
5. Or22a-GAL4/UAS-*rpr* mutant *Drosophila* lack ab3 cells indicating that Or22a/b is expressed in ab3A neurons, which are known to be sensitive to ethyl butyrate (Carlson Declaration, paragraph 7).
6. Deletion mutants lacking Or22a/b display severely reduced response to ethyl butyrate (Carlson Declaration, paragraph 8).
7. The wild-type response to ethyl butyrate is fully rescued by supplying a transgenic wild-type copy of Or22a, consistent with a function for Or22a in binding ethyl butyrate (Carlson Declaration, paragraph 8).

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The evidence provided in the Carlson Declaration and the Figures A-G associated with the Carlson Declaration clearly demonstrate that the protein encoded by SEQ ID NO: 31 is an olfactory receptor, thus establishing the sequence-to-function relationship required by the Examiner in this rejection.

The Office Action further indicates that the use of a protein for identification of substances which inhibit its activity has been determined by the courts to be a non-patentable utility. The Examiner is respectfully requested to provide a citation to the decision supporting this statement. Applicants respectfully submit that the identification of binding partners for an isolated protein, wherein that binding partner has a well-established role in cellular responses as here, provides a patentable utility to the receptor to which it binds. See, for example, *Cross v. Iizuka* (1985) Fed. Cir. 753 F.2d 1040, holding that evidence of *in vitro* testing may be used to establish utility. Certainly, the results set forth in the Carlson Declaration involving deletion mutants lacking Or22a/b clearly demonstrate the odorant receptor function of the Or22a protein encoded by SEQ ID NO: 31.

The clearly established odorant receptor function of SEQ ID NO: 31 as taught by this invention leads one to many utilitarian purposes to which this sequence can be applied. For example, the specification teaches that the claimed nucleic acids are useful in identifying agents which affect odorant receptor activity (see page 36, line 25 to page 38, line 20). The specification also discloses the preparation of both monoclonal and polyclonal antibodies using the odorant receptors of the invention as an antigen to produce these antibodies (see page 37, line 11 to page 38, line 14). The specification also discloses that the claimed odorant receptors can be used in studying means to modify *Drosophila* insect behavior (see page 47, line 20 through page 48, line 2). More specifically, the claimed odorant receptors may be used to study mating enhancement/disruption (page 49, lines 7-12), and attraction/repulsion (page 49, line 18 to page 50, page 19). There are abundant utilities for the claimed receptors, as set forth herein and in the specification, including pesticide design, insect trapping, insect baiting, and the like. Enterprises such as these are important to basic human needs including the raising of crops, the production

of ornamental flowers and controlling the spread of insect-borne diseases (*e.g.*, through controlling disease bearing pests, such as mosquitoes).

In light of the aforementioned remarks; the strong establishment of the structure-to-function relationship as taught in the specification, the Carlson Declaration and herein; and the newly added claims, Applicants respectfully request that the rejection be withdrawn as it applies to the pending claims.

Response to the rejections under 35 U.S.C. 112 (first paragraph)

Claims 1-10 were rejected under 35 U.S.C. 112 (first paragraph) purportedly because the specification is not enabling for a nucleic acid encoding a fragment of a *Drosophila* odorant receptor protein.

Applicants have canceled claims 1-10 and added new claims 27-45. The amino acid fragments claimed in claim 27 are those that include specific extracellular domains encoded by SEQ ID NO: 31. The fragments claimed in claim 45 are having at least 25 consecutive amino acids of SEQ ID NO: 31 and odorant receptor activity. The specification provides multiple representative examples of nucleic acids encoding an odorant receptor protein fragment (see page 17, line 28 through page 18, line 17). In addition, as established by the specification and the Carlson Declaration, one skilled in the art can use well-established protocols to test whether a claimed fragment has odorant receptor activity. For these reasons, the Examiner is respectfully requested to withdraw this rejection as it applies to the now pending claims.

Response to the rejection under 35 U.S.C. 112 (second paragraph)

Claims 1-10 were also rejected under 35 U.S.C. 112 (second paragraph) as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. The Office Action indicates that the term "sufficient stringency" recited in claim 1 is unclear as to which conditions are necessary to produce a clear signal.

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While the conditions of sufficient stringency to produce a clear signal are defined in the specification on page 17, lines 10-24, Applicants have nonetheless canceled claims 1-10 so as to remove the aforementioned language. Newly added claims 43 and 44 clearly provide the stringency conditions used to identify the claimed nucleic acid sequences as set forth in the specification in Example 2, pages 60-61. In light of these amendments, Applicants respectfully request that the rejection be withdrawn.

Response to the rejection under 35 U.S.C. 102(a)

Claims 1-10 were rejected under 35 U.S.C. 102(a) purportedly for being anticipated by Celniker *et al.* (1998) (GenBank Accession No. AC004121). This reference purportedly provides a protein fragment of at least 6 amino acids in length that would hybridize to the previously-claimed sequences to produce a clear signal.

In an effort to expedite prosecution, Applicants have canceled claims 1-10. As discussed above, newly added claims 27 and 45 are directed to specific amino acid fragments encoded by the nucleic acids of SEQ ID NO: 31.

Applicants respectfully submit that the cited art does not disclose all of the limitations of the pending claims because it does not disclose any exon-intron boundaries of SEQ ID NO: 31, nor an open reading frame, nor a fragment of at least 25 consecutive amino acids of SEQ ID NO: 31, for the disclosed nucleic acid sequence. Applicants respectfully request that the rejection be withdrawn in light of the amendments.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at his convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted
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